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MEDICAL DEVICES

Good Manufacturing Practice Regulations for Manufacture, Packing, Storage and Installation

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[21 CFR Part 820]

[Docket No. 75N-0140]

MEDICAL DEVICES

Good Manufacturing Practice Regulations for Manufacture, Packing, Storage, and Installation

The Food and Drug Administration (FDA) is proposing good manufacturing practice (GMP) regulations for the manufacture, packing, storage, and installation of medical devices under section 520(f) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j(f)). Comments are requested by June 29, 1977.

In addition, the Commissioner of Food and Drugs is proposing to make the final regulation effective 90 days after the date of publication of the final regulation.

On May 28, 1976, the Medical Device Amendments of 1976 (Pub. L. 94-295) were enacted into law, amending the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 201 et seq.). Section 520(f) of the act provides the agency with authority to prescribe regulations requiring that the methods used in, and the facilities and controls used for, the manufacture, packing, storage, and installation of medical devices conform to current GMP requirements. These proposed regulations are designed to assure that devices will be safe and effective for their intended use and otherwise in compliance with the act.

Under section 520(f)(3) of the act, the Commissioner must establish an advisory committee for the purpose of advising and making recommendations to him with respect to these regulations. Under this provision, the Commissioner is authorized to request recommendations from this advisory committee on any petitions submitted requesting exemptions or variances from GMP requirements. The Device Good Manufacturing Practice Advisory Committee (GMP Advisory Committee) will review and comment on the proposed current good manufacturing practice rules prior to publication of the final regulation. A notice requesting nomination for members of this committee was published in the FEDERAL REGISTER of July 13, 1976 (41 FR 28817). A notice of establishment of the GMP Advisory Committee was published in the FEDERAL REGISTER of August 27, 1976 (41 FR 36233) giving the details of the charter of this advisory committee.

Since December 1973, FDA has been involved in the development of current GMP regulations for medical devices. A concerted effort has been made by FDA to involve individuals and associations representing industry, health professionals, and consumer organizations in the development of GMP regulations. The Food and Drug Administration has also attempted to stimulate representatives of the industry to develop a number of unique GMP regulations applicable to specific types of devices. This endeavor was aided by technical and compliance experts from FDA headquarters and field offices who had background and experience relative to the regulation of the industry. The Food and Drug Administration then consolidated various draft proposals into a single draft regulation (an umbrella GMP) applicable to the entire device industry.

A notice of availability of the draft regulations was published in the FEDERAL REGISTER of August 8, 1975 (40 FR 33482). Interested persons were provided 60 days in which to submit comments. While the responses to the notice of availability varied, it was apparent that the interest in this subject is intense. The Food and Drug Administration distributed more than 3,000 copies of the draft regulations, and additional copies were reprinted and distributed by trade associations and the trade press. In view of the interest generated by the draft regulations and after a review of the initial comments, it became evident that the scope of the usual open public process should be broadened to provide for direct exchange of information between FDA and those persons concerned with the potential impact of GMP regulations. Therefore, FDA published in the FEDERAL REGISTER of October 9, 1975 (40 FR 47530) a notice announcing four public meetings to be held across the country to give interested persons the opportunity to present data, technical information, and views concerning the draft current GMP regulations. These meetings, which were held in November 1975 in cooperation with the Dallas, San Francisco, Chicago, and Baltimore District Offices of FDA, consisted of a preliminary interpretation of the draft regulations by a panel of FDA officials, followed by an open question and answer session during which the panel entertained specific questions, comments, and suggestions from the attendees. Approximately 1,200 persons attended these four meetings, and all questions and comments were recorded and transcribed.

In addition, 130 written comments responding to the draft regulations have been received and reviewed by FDA. These comments were received from a broad cross section of small and large firms that manufacture devices ranging from the relatively simple to the extremely complex.

In addition to comments received directly from manufacturers, FDA received responses from various trade and professional associations including the American Dental Trade Association; American Surgical Trade Association; the Compressed Gas Association; Coalition of Independent Ophthalmic Professionals; Pharmaceutical Manufacturers Association; Health Industry Manufacturers Association; National Electrical Manufacturers Association; Optical Manufacturers Association; Optical Wholesalers Association; Orthopaedic Surgical Manufacturers Association; and the Scientific Apparatus Makers Association. Comments were also received from industry consultants, attorneys, and representatives of academic institutions. All comments received and the transcripts for each of the four public meetings are on display in the office of the Hearing Clerk, Rm. 4-65, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

The Commissioner has reviewed both the written comments received in response to the notice of availability of the draft regulations and the transcripts of each of the four public meetings. He finds that the majority of comments are general in nature, i.e., primarily concerned with such issues as the overall concept of umbrella GMP regulations and their intended scope; the costs versus benefits associated with their implementation; descriptions of the manufacturing practices currently being employed within the industry; and the repercussions anticipated subsequent to the promulgation of such regulations. Although specific objections and tenable alternatives to the various measures proposed in the draft regulations were not generally contained with these comments, the Commissioner believes that the comments provided valuable information.

The Commissioner recognizes that the medical device industry consists of manufacturers whose devices and manufacturing processes differ significantly. This diversity of manufacturing processes affects the development of comprehensive GMP regulations equally applicable to all. Therefore, the Commissioner believes that GMP regulations applicable to all manufacturers should not be so specific as to indicate to every type of device manufacturer what he must be doing and how such manufacturing practices must be undertaken. Rather, the proposed GMP regulations should contain general requirements applicable to all manufacturers and fewer specific procedures than were enunciated in the draft regulations. The proposed umbrella GMP regulations identify specific areas of concern with the intent that the manufacturer will supply the details which, in his judgment, are appropriate for his device. This will mean that each specific device manufacturer should develop for the manufacture of such device a detailed set of procedures which implement the GMP regulations in this proposal. Such procedures will be used by FDA to determine whether a manufacturer is complying with the intent of these regulations.

The Food and Drug Administration expects to publish subsequent GMP regulations applicable to specific types of devices, thereby supplementing the umbrella GMP regulations. These GMP regulations will be of two types: One will contain requirements that will apply only to generic devices or individual classes of devices (e.g., pacemakers, eyeglasses, etc.); the other will contain requirements that will apply to certain devices or cross-class characteristics or processes (e.g., sterile devices, plastics, electrical properties, etc.).

The Commissioner believes that umbrella GMP regulations should distinguish between devices that are used to

support, sustain, or prevent impairment of human life or health, or that could present an unreasonable risk of illness or injury in the event of failure (critical devices) and those which do not (noncritical devices). This distinction has been incorporated into the proposed regulations by means of a two-tier approach which denotes general requirements applicable to all devices (critical and noncritical) and specific requirements applicable to only those devices classified as critical. The entire regulations are applicable to critical devices. The sections designated critical devices are applicable only to critical devices. Because of this two-tier approach, it is necessary that the terms "critical" and "noncritical" be meaningful and well understood. Therefore, the Commissioner is particularly interested in the response to the definition for critical device in proposed § 820.3.

The subpart in the draft regulations concerned with sterility (Subpart L) is deleted from the proposed regulations. Sterility requirements are technical and must be separated from an umbrella GMP, which is general. Sterility requirements apply to cross-class processes and will be addressed in a subsequent GMP regulation to be proposed in the FEDERAL REGISTER at a later date. Those comments concerning sterility made in response to the draft regulations will be discussed at the time the GMP regulation for sterile devices is proposed.

A number of comments agreed with provisions of the draft regulations and are therefore not addressed in the preamble to this document. Based on the comments received on the draft regulations and agency review, several other changes are made. A discussion of these changes is provided as follows:

GENERAL PROVISIONS

1. Two comments regarding the paragraph on "Limitations" indicated that the draft GMP regulation was too stringently written to apply as an umbrella GMP to all devices as a minimum requirement. It was requested that requirements for those devices whose failure in normal use would present an unreasonable risk of injury to the patient or user should be covered in a separate part applicable to specific product and class GMP's.

The Commissioner recognizes the problem raised in the comment and accordingly has specified more rigorous requirements for critical devices than noncritical devices as discussed in the two-tier approach above.

2. Three comments regarding the paragraph on "Applicability" noted that the cost of assuring the compliance of foreign manufacturers would be prohibitive to such an extent that inspections would be minimal, if at all, giving the foreign manufacturer a decided advantage over the domestic medical device industry.

The Commissioner rejects these comments. The same degree of control will be exerted over imported medical devices as that for domestic medical devices. The device GMP regulations apply to any device imported or offered for import into the United States. Devices which are questionable with respect to safety and effectiveness will be detained upon importation unless FDA is able to make the inspectional observations necessary to assure their safety and effectiveness.

DEFINITIONS

1. One comment suggested deletion of the definition of "automated quality control" which was defined in the draft regulation as "any computer or apparatus that performs quality control functions independently or semi-independently of manual control, and performs a decisionmaking function." The comment suggested that the definition was unnecessary because of the separate treatment given quality control and automated quality control in the draft GMP regulations. Several other comments recommended deletion of that part of the definition which implied that decisionmaking functions are performed by automated quality control equipment. It was emphasized that men make decisions and that computers do not.

The Commissioner rejects the comments suggesting deletion of the definition of "automated quality control" because he finds that such a definition is necessary to give the fullest understanding of the term as it is used in the proposal. The Commissioner agrees with the comments pertaining to decisionmaking functions being performed by automated quality control equipment and has modified the proposed definition accordingly.

2. Several comments suggested changing the part of the draft regulation which defined "component." It was asserted that the phrase "or any article or material intended for use in conjunction with the finished product" was redundant. Two additional comments suggested that "component" be defined as "any article or material used in the manufacture of a device which will appear in the finished product or any article or material specified by the manufacturer for use in conjunction with the finished product."

The Commissioner agrees with the comments and has incorporated the substance of the comments in the proposed definition.

3. Two comments suggested deleting part of the paragraph that defined "control number" as "any distinctive numeric or alphanumeric character(s), from which the complete history of manufacture, control, packaging, sterilization, and distribution of the device(s) can be determined." It was asserted that the phrase "from which the complete history of manufacture, control, packaging, sterilization, and distribution of the device(s) can be determined" could be construed as specifying the required use of a control number. It was suggested instead that "control number" be covered in the operating provisions of the GMP regulations.

The Commissioner disagrees with the comments and has specified the mandatory use of control numbers for critical devices and critical components. The use of control numbers for noncritical devices is optional. The Commissioner rejects the comments suggesting the deletion of the definition of "control number" because he finds that such a definition is necessary to give the fullest understanding of the term as it is used in the proposal. Several additional comments suggested that the definition for "control number" should be "any distinctive code designation from which a product/component could be traced subsequent to its manufacturing and distribution cycle."

The Commissioner disagrees with the comments because he finds the specific terms used in the proposed definition such as components, control, packaging, sterilization, production run, lot, batch, date code, or serial number are necessary to give the fullest understanding of the term as it is used in the proposal.

4. Several comments were received on "critical component" which was defined as "a component which, if defective or improperly manufactured in any manner or otherwise unsuitable for use, can be expected to unreasonably affect the safety or effectiveness of a device, and is of such a nature that it is feasible to individually identify." A few comments considered the definition of critical component too restrictive. It was suggested that this concept be deleted from an umbrella GMP and placed instead in the specific product and class GMP's for those products which have significant patient or user hazard. Two other comments would define "critical component" as a component which has a potential for failure, the occurrence of which would create a hazard to the safety of the patient or user and as such, would not be disclosed by normal quality control procedures.

The Commissioner has restricted the use of the term critical component to critical devices and has proposed a new definition which combines the substance of the draft definition and the definitions suggested above.

5. Several comments suggested alternative definitions for "critical operation," which was defined as "any operation in the production of a device that, if incorrectly done, contains a high potential for failure of product requirements of safety and effectiveness." It was suggested that "critical operation" be defined as any operation in the production of a device that, if incorrectly done, contains a high potential for failure of product requirements for safety and effectiveness essential to the health and physical welfare of the patient or user.

The Commissioner has restricted use of the term "critical operation" to critical devices and has proposed a new definition, which combines the substance of the draft and the definition suggested above.

6. One comment was received on the paragraph that defined a "quality control unit" as "any organizational element of the manufacturer having the authority and responsibility in accordance with § 810.20 (proposed § 820.20), to approve or reject components, in-process materials, packaging materials, and final products." It was suggested that this definition should be revised to take into con-

sideration two quality groups—quality control and quality assurance—as each is normally found in the corporate structure.

The Commissioner rejects the suggestion as the definition does not mandate the nomenclature of the organizational structure the manufacturer may wish to utilize. The Commissioner is concerned only that the organizational element of the manufacturer have the authority and responsibility in accordance with proposed § 820.20.

One additional comment asked how the draft definition of "quality control unit" will apply to custom manufacturers who may be building devices to customer specifications.

The Commissioner intends that custom manufacturers comply with the regulations. Custom manufacturers are directed to section 520(f) of the act, which authorizes persons subject to GMP requirements to petition the Secretary for an exemption on variance from one or more of the regulations.

7. Several comments suggested definitions for the following terms: "recondition," "repair," "complaint," "labeling," "labels," "sterility," "package," "manufacturer," and "manufacturing material."

The Commissioner has defined those terms necessary to clarify the regulations. These include definitions for the terms "manufacturer" and "manufacturing material." The term "complaint" is explained in proposed § 820.198. The terms "label" and "labeling" are defined in the act. The term "sterility" is deleted in favor of a specific GMP regulation for sterile devices to be published in the FEDERAL REGISTER at a later date. Other suggested terms do not require a definition since the meaning provided by a dictionary is sufficient. The Commissioner has proposed the following definitions that were not included in the draft regulations:

"Critical device" has been defined because of the importance of the term and its extensive use in the proposed regulations.

"Finished device" has been defined to distinguish between a device and a component.

"Manufacturer" has been defined to differentiate between a manufacturer and a distributor.

"Manufacturing material" has been defined to distinguish between manufacturing materials and a component.

"Noncritical device" has been defined to distinguish between critical and noncritical devices.

ORGANIZATION AND PERSONNEL

1. Several comments objected to the requirement in the draft regulations that the quality control unit and the production unit be organizationally and functionally independent of each other. It was suggested that this requirement ignored the practical realities existing within small manufacturing operations, in that production personnel at the plant level in small firms often serve as quality control inspectors and that to do otherwise in such firms would make production costs prohibitive. Several additional comments argued that GMP regulations should not dictate organizational structure but should, instead, require device manufacturers to document their organizational structure with clearly defined responsibilities and authority in regard to controls and product acceptance.

The Commissioner's intent is not to dictate organizational structure. He agrees that this regulation might cause problems within small manufacturing operations. It is felt that separation of the production and quality control functions is of the utmost importance, regardless of organizational size. The intent of the regulation is to clearly establish and delineate the authority and responsibilities of persons and organizations performing quality control operations. The proposed regulation now allows organizational flexibility while requiring responsibility and authority for implementation of a quality assurance program to be given to a quality control unit. Additionally, the Commissioner has deleted the draft regulation exempting small firms from certain requirements of the proposed regulations.

2. Several comments suggested deletion of the requirement that periodic quality control audits be made by a qualified individual to verify compliance with all aspects of the quality assurance program. It was interpreted that the regulation required and legislated a special audit of the quality assurance system which, by its nature, should be self-auditing on a continuous basis.

The Commissioner rejects the comments because he finds that systematic and periodic audits should verify compliance with all aspects of the quality assurance program and that these audits should be done by individuals not having responsibilities in the area audited.

3. A few comments suggested deletion of the draft regulations that required each employee to undergo orientation for each function that he or she performs, as well as deletion of the requirement that personnel performing aseptic techniques be trained by persons qualified in that field. It was felt that these two areas were covered without further delineation by the requirements for training in the introductory statement in this section.

The Commissioner agrees with the comments and has revised the proposal accordingly.

4. Several comments suggested deletion of that portion of the draft regulations regarding employees' personal health. It was suggested that this reference to individuals' personal health placed on the manufacturer the responsibility for the diagnosis and detection of illness in employees.

The Commissioner rejects these comments because it is important to exclude from the manufacturing process employees who exhibit diagnosed or apparent illness which may have an adverse effect on the product. The Commissioner has, however, deleted the reference to open lesions, as specific references to pathological conditions are not necessary because of the reference to "diagnosed or apparent illness" in the proposed regulation.

BUILDINGS

1. Several comments recommended deletion of the requirement that facilities be of suitable size, construction, and location to carry out adequately the manufacturing process. It was felt that these requirements are not directly related to product safety features. It was noted that many of the requirements must be fulfilled for compliance with occupational safety requirements. Additionally, a few comments argued that the size, construction, and location of a building, as used in the draft regulation, may or may not affect device manufacturing.

The Commissioner rejects these comments because it is felt that manufacturing conditions relative to building design and space may affect the safety and effectiveness of a device. This subpart has been retitled "Buildings" because "buildings" is the term used throughout the proposed regulation.

2. Several comments recommended rewording of the requirement in draft § 810.46 that environmental factors "be controlled to prevent contamination and provide proper conditions for the storage, manufacture, assembly, packaging and labeling operations for each product." It was suggested that the proposed regulation be stated as follows: "The environmental factors, to the extent that they adversely affect the safety and performance of the product, be controlled as follows (list of factors)." It was believed that this change would clarify the intent that only those environmental factors that could adversely affect the safety and performance of a device be subject to this regulation.

The Commissioner agrees and has incorporated the substance of the comment in the proposed regulation by inserting the words "when necessary." This is to ensure that the environmental factors listed are controlled only where they are a factor in product or process operation.

3. Several comments concerning environmental control suggested that explantions for each environmental factor were redundant. They offered the following rewording:

The environmental factors shall be controlled to minimize contamination and to provide adequate conditions for the storage, manufacture, assembly, packaging, and labeling operations for each product. Environmental factors to be given consideration, depending on the product or process involved, include: lighting, ventilation, temperature, humidity, air pressure, laminar air flow, screening and filtration and environmental testing.

The Commissioner agrees with the comments and has revised the substance of the proposed regulation accordingly.

4. A few comments objected to the requirement that adequate cleaning and sanitation meet product or process requirements. It was felt that the Occupational Safety and Health Act regulations extensively detail occupational safety and health requirements. It was suggested that deletion of this section would avoid the potential for conflicting regulations.

The Comissioner has determined that Occupational Safety and Health Act regulations do not include all of the cleaning and sanitation requirements stated in this GMP proposal. Although there are some areas of common interest, the Commissioner is not promulgating conflicting regulations. The scope of these regulations, as set forth in the "General Provisions" subpart of this document, necessitates requirements to assure the safety and effectiveness of devices. The Occupational Safety and Health Act regulations do not have this intent.

EQUIPMENT

1. Many comments suggested deletion of the draft regulation requirement that "There shall be for each piece of equipment a schedule of maintenance, adjustment, and cleaning that is appropriately related to the function of the equipment."

The Commissioner accepts the comments and has revised the proposed regulation to require scheduled maintenance, adjustment, and cleaning only where applicable.

Many comments suggested deletion of the draft regulation requirement that "For each piece of equipment subject to adjustment there shall be visibly posted in a prominent place on or about the equipment, a specification of the allowable tolerances within which the equipment performs its function." It was asserted that the maintenance of machine tolerances should not be imposed by legislation. It was argued that since the finished product is manufactured within stated tolerances, it is this tolerance that is important.

The Commissioner rejects the comments because it is necessary to monitor the quality of a device throughout the manufacturing process and not just at the point of finished device testing. The tolerance of a machine manufacturing a device is a quality point to be monitored on a schedule that is documented when performed. However, the Commissioner has modified this requirement so that the schedules are only required if applicable for the equipment.

2. Several comments recommended deletion of the requirement that the device should not be adversely affected by contact with equipment surfaces beyond established and documented limits.

It was noted that the introductory paragraph to the draft regulation stated that equipment should "be suitable" for its intended purpose and that this phrase defines the intent while allowing enough flexibility and interpretation for an umbrella GMP regulation.

The Commissioner accepts the comments and has deleted the specific surface design requirements in the proposed regulations.

3. Several comments objected to the requirement that quality control instruments and measuring equipment be appropriate for measuring the test parameter and conform to laboratory standards whose calibration is traceable to the prime standards at the National Bureau of Standards, U.S. Department of Commerce. It was pointed out that not all testing equipment has a calibration traceable to the National Bureau of Standards. It was recommended that the phrase, "where appropriate" be added at the end of the sentence.

The Commissioner agrees with the comments and has added the following alternatives to proposed § 820.62: "If prime standards do not exist for the parameter being measured, an independent reproducible standard shall be used. If none of the above exists, an in-house primary standard shall be developed and used."

4. Several comments objected to the specific language of the requirement for performing measurements, namely: "* * * the accuracy of the measurement equipment shall be added to the measured deviation from nominal and the sum shall not exceed the allowed tolerance for that parameter." It was contended that this regulation specified the accuracy these measurements must meet and that the added economic impact for these calculations would be prohibitive.

The Commissioner accepts the comments and has deleted this requirement from the proposal.

5. Several comments suggested deletion of the requirement that a determination be made of the validity of the design of, equipment used for, and/or programming used in an automated quality control process. It was asserted that this is a specialized area of limited applicability and, therefore, not appropriate in an umbrella GMP; the requirement is superfluous because it states the obvious; and that automated quality control equipment should meet the same requirements as other instrumentation and measuring equipment.

The Commissioner rejects the comments because automated quality processes are used for many devices covered under the umbrella GMP and therefore should be proper subject matter for this proposed GMP. The Commissioner agrees that this requirement states the obvious as does the entire regulation. However, the obvious to some is not the obvious to everyone, and the need for a regulation reiterating basics is apparent. The Commissioner believes that there are elements of automated quality control that are not present in manual systems and these additional elements should be regulated accordingly.

6. Many comments contended that required semiannual calibration for each piece of equipment was an unjustifiable and unreasonable economic burden. It was argued that such a requirement was inappropriate in an umbrella GMP regulation. Reference was made to military specification MIL-C-4566A which sets forth requirements for calibration systems without recommending a fixed maximum calibration level.

Several additional comments on calibration scheduling noted that these regulations cover a broad scope of device manufacturing equipment, including some equipment not requiring recalibration. It was proposed that the regulation be restated to require recalibration of each piece of equipment in accordance with an established schedule for that piece of equipment.

The Commissioner agrees with the comments and has modified the proposed regulation to require routine calibration of automatic, mechanical, or electronic measurement equipment.

CONTROL OF COMPONENTS, CONTAINERS, AND IN-PROCESS MATERIALS

1. Several comments concerning critical components contended that unless a more specific definition for critical components can be agreed upon, all references to "critical" components and "critical" operations should be deleted from the GMP regulations.

The Commissioner has redefined the terms "critical components" and "critical operations" in the proposal. The proposed regulations have been revised to restrict the use of these terms to sections of the regulations specifically dealing with critical devices.

2. Many comments suggested deletion of the requirements that personnel responsible for quality control of incoming components maintain a continual record of rejection percentages in an acceptance trend record. It was argued that such a requirement has no bearing on the performance of a product and is not appropriate to good manufacturing practices; it is a management tool not properly the subject of GMP's; it is costly recordkeeping that does not contribute to the assurance of safety or performance; it is a prerogative of the manufacturer and, as such, should not be legislated.

The Commissioner agrees with the comments as they apply to noncritical devices but believes such a record of supplier performance is essential for critical devices. Accordingly, the Commissioner has modified the regulation to make it applicable to critical devices only.

3. Several comments suggested deletion of the statement that the manufacturer is ultimately responsible for the quality and compatibility of all components made or supplied to him. Such a requirement could be interpreted to mean the manufacturer is solely responsible if a problem arises. It was noted that such is not the case under the act nor under the current product liability law. The comments indicated that such an interpretation would tend to limit legal remedies available to consumers and finished product manufacturers in a liability suit.

The Commissioner accepts the comments and has revised the proposal so that specific responsibility for component failure is not assigned.

4. Several comments addressed the requirement that a written agreement exist between the supplier and manufacturer providing for notification of changes made in components. The comments contended that it would be unreasonable, inefficient, costly, and impractical for the supplier to notify the manufacturer of changes made in each component of a noncritical nature.

The Commissioner agrees with the comments and has revised the proposal to apply to critical devices only.

PRODUCTION AND PROCESS CONTROLS

1. Several comments objected to the requirement in the draft regulation that "a critical operation performed manually shall be performed by a responsible and competent individual, and shall be checked by a second responsible and competent individual." Deletion of this requirement was recommended because the draft regulations on "Personnel" state that all employees must have capabilities commensurate with their assigned functions. It was asserted further that the performance of a capable person need not be checked by a second person.

The Commissioner rejects the comments because he believes that thorough verification is necessary for critical device manufacture. However, the proposed regulations have been amended to require verification for any critical operation by designated individuals or equipment.

2. Several comments recommended deletion of the requirement that a formal approval procedure for any change contemplated in the manufacturing and assembly process of a product be included in the master product record. It was suggested that a reference to the change approval procedures be permitted instead of inclusion of the actual document in the master product record.

The Commissioner agrees with the comments and has incorporated the substance of the suggestion into the proposed § 820.181 on Master Device Records.

PACKAGING AND LABELING CONTROL

1. Many comments believed that the regulations on labeling control were patterned after controls needed for the drug industry. It was implied that they are far too stringent for most medical devices and the imposition of unnecessary steps and restrictions would serve no useful purpose and would only increase the cost of the product.

The Commissioner has revised the regulations for critical device labeling to include the following controls: labeling receipt, storage, access restriction, and excess printed labels. This reflects the Commissioner's concern that critical device labeling operations be strictly controlled to prevent labeling mixups. However, the Commissioner has agreed with the comments in regard to noncritical devices and has modified the requirements for labeling of these products.

2. A few comments recommended rewording the requirements that containers and packages be suitable for their intended use and that such containers and their components may not adversely affect the device. It was suggested that the proposed regulation require product containers or packages to adequately protect the product from reasonably expected external factors that could alter or damage the product.

The Commissioner rejects the comments as applied to critical devices because the suggestion is too general to implement the intent of the regulation. However, he accepts the comments as applied to noncritical devices.

HOLDING AND DISTRIBUTION

1. Several comments objected to the specific language of the draft regulation which required a stock rotation system whereby the oldest approved products were distributed first. It was contended that such a requirement ignores the purpose of expiration dating and assumes that such dating will be ignored by the intended user. Additionally, the comment stated that a customer who wanted an entire lot of a particular product would be prohibited from purchasing it if there wree products still available from a previous lot.

The Commissioner agrees with the comments and has modified the proposed regulation to require stock rotation where appropriate.

2. Many comments recommended deletion of the requirement that adequate distribution records, including the names of the initial and all subsequent known consignees, be maintained and be readily available.

Deletion of the requirements concerning "all subsequent consignees" was suggested because of the following reasons: Only the initial consignee should be responsible for maintaining records for subsequent consignees; manufacturers are in no position to know the identity of subsequent consignees; when selling through dealers, it is impossible to know more than the initial consignee for a long-lived product; this could be interpreted to mean that any time a manufacturer learns where one of his products is subsequently consigned, he must rush to his distribution records and record the name of the subsequent consignee; this could cause havoc with good recordkeeping and would impose a burden on the manufacturer, and the varied nature of medical device distribution makes compliance with this requirement difficult.

The Commissioner agrees, in part, with the comments and has deleted the requirement concerning distribution recordkeeping for noncritical devices only. This reflects his concern that critical device distribution records be readily available in the event of recall or other actions.

PRODUCT EVALUATION

1. Many comments suggested deletion of the requirement that each control number unit of production be retained prior to final product inspection for a sufficient period of time to allow the final product inspection to validly reflect the state of the product upon reaching its point of use.

It was stated that, as written, this regulation is confusing and contradictory; it describes redundant requirements in the master product record and the product history record; product retention or holding is part of the manufacturing procedure; some products undergo changes for long periods or throughout their life; and such a measurement will not assure that the product reaches the end-user in satisfactory condition.

The Commissioner accepts the comments and has deleted the requirement from the proposed regulation. However, the proposed regulations now require devices to be tested under operating conditions.

2. A few comments recommended deletion of the requirement that each number control unit of production of a product be fully tested, before release for distribution, for conformance with all requirements and specifications of safety and effectiveness established for the product. These comments contended that the requirement would be very costly and unnecessary.

The Commissioner rejects the comments because it is believed that final product testing reduces the incidence of faulty components or products, thereby lessening the possibility of injury to the user.

3. Several comments objected to the requirement that, upon completion of final product inspection, the control number unit of production shall not be released for distribution until all records and test results are checked by a responsible authorized individual. It was argued that final product release should not be dependent upon a single individual, assuming that all records and documentation are present, complete, and correct. Instead, individuals should be responsible for verifying all such documentation approval by authorized personnel along the manufacturing process.

The Commissioner rejects the comments because he finds that this type of responsibility should be a single, conscious act and should not be shared at intermittent time intervals. The Commissioner has proposed finished device release for critical devices by a designated individual who is responsible for releasing the device.

RECORDS AND REPORTS

1. Several comments objected to the requirement that all obligatory records be marked and separated into confidential and nonconfidential portions to aid FDA in determining which information retained or acquired by the agency is releasable under the Freedom of Information Act. It was asserted that this section is not relevant to GMP's; confidentiality is adequately defined and treated under the Freedom of Information Act and under 21 CFR Part 4; in addition to excessive documentation, this requires prior segregation of records on a continual basis for potential FDA release to the public.

The Commissioner rejects the comments because he believes that this requirement is relevant to GMP's as it applies to manufacturers' GMP records. Additionally, this regulation does not require excessive documentation, but, instead, requires the marking of already existing records. These records may be marked continually, sporadically, or not at all; specifics are left to the manufacturers discretion.

2. Many comments recommended changing the requirement that mandated the retention of all required records per-

taining to a product for a period of 2 years or the intended or actual known life of the product, plus 1 year, whichever is longer. It was believed that a limiting time should be established, and it was felt that 2 years was an adequate period for an umbrella GMP applicable to all devices.

The Commissioner rejects the comments but has revised the proposal to allow the manufacturer to designate the criteria for determining the record retention period, which shall be at least 2 years.

3. Many comments objected to the requirement that copies of all promotional material be included in the master product record. It was contended that inclusion of any promotional material in labeling control regulations added extra and unwarranted work unrelated to labeling control.

The Commissioner rejects the comments. He believes that controls on promotional material should be retained because claims could appear in promotional material that could change labeling requirements.

Several comments recommended deletion of the references to labels and labeling from the master product record. It was believed that this requirement was redundant since these are requirements under product specifications. It was also suggested that labels and promotional materials should not be a part of the master product record because these items are subject to constant change.

The Commissioner rejects the comments because the regulation does not require a duplication of labels and labeling in two different sections of the master device record. Approval of labels and labeling by designated persons is required. The approved material should then be placed or referenced in the master device file. The Commissioner feels the constant change mentioned in the comments necessitates the existence of a master device record with approved labeling material. There must be a primary source document for production personnel to use a reference so that old or inaccurate labels are not used inadvertently.

4. Several comments objected to the requirements that a product history record be prepared. It was maintained that not all devices require the same degree of control and that the draft regulation required extensive record development and retention well beyond the value returned. It was suggested that the requirement would be more appropriate in a specialized product GMP regulation, not an umbrella regulation.

The Commissioner has revised the regulations on device history records mandating specific requirements for manufacture of critical devices while the requirements for noncritical devices have been generalized.

Many comments contended that maintenance of the product history record in one location was impractical and unnecessary.

The Commissioner accepts the comments and is not requiring the cited records to be in one location. However, critical device final inspection requires that such records for critical devices be present, complete, and correct prior to distribution.

5. Several comments objected to the requirement in the draft regulation that design documents must be verified. It was stated that such a requirement is impractical, unnecessary, and is not a GMP.

The Commissioner agrees with the comment and has deleted such a requirement from the proposed regulations.

6. Many comments recommended deletion of the requirement that there shall be a written quality control manual for each product with at least one copy of the manual in each production area. It was stated that this kind of information is usually kept in category files; industry does not now have such manuals and this requirement would be an economic burden; much of the information provided would be redundant; and quality control procedures should be made a part of the master product record.

The Commissioner rejects the comments because he finds that the degree of control required for critical devices justifies specific requirements such as those found in the quality control manual. Information located in the manual such as sampling plan, formal change approval, and inspection checks would be extraneous if located in the master device record because those operations involve only quality control personnel. Accordingly, the Commissioner has revised the proposed regulations making specific requirements for critical device manufacturers, but has generalized requirements for noncritical devices.

7. Several comments objected to the requirements concerning dual records, programming, data input, and access security relative to automatic data processing. It was felt that the regulations attempted to fix responsibility and define the steps required so closely so as to prevent the exercise of necessary authority. They further felt this to be a management tool and its use a management prerogative.

The Commissioner agrees that this regulation fixes responsibility and is a proper objective of a regulation. However, the regulation has been rewritten to give management more latitude in the implementation of the regulation. The regulations for automatic data processing have also been revised to make this a requirement applicable only to critical devices. The Commissioner believes the degree of control needed for critical devices justifies this requirement.

8. A few comments recommended that the draft regulation concerning complaint files be rewritten to require written procedures and maintenance of records of all user reports to the manufacturer pertaining to injury, death, or any hazard to safety. It was also felt that records of such safety complaints should be located at, but not limited to, a centralized location where the responsibility for investigation resides.

The Commissioner rejects the comments as inadequate for the protection of the consumer. In addition to concerns about injury, death, and hazard to safety, the Commissioner believes the complaint files should also include any expressions of dissatisfaction regarding the identity, quality, durability, reliability, effectiveness, or performance of a device.

The Commissioner also finds it necessary that manufacturers maintain complaint records at the device manufacturing site because it is sometimes necessary to interview employees and review records concerning manufacturing failures resulting in complaints.

A few comments felt that the requirement that complaint files include all complaints creates the additional burden and cost of maintaining excessive files. They believed that the bulkiness of the file would be a reflection of a company's success in the marketplace. This information would be available to the manufacturers' competitors through the Freedom of Information Act and would be of limited value for consumer protection.

The Commissioner rejects the comments because it is believed that the number of complaints a manufacturer receives is more directly proportional to product design and adequate quality assurance systems that the total number of customers. Trade secrets are protected through provisions of the Freedom of Information Act and consumer interests are best served through the monitoring of complaint files.

9. Many comments objected to the requirement that reworked products attain the same level of quality, safety, and effectiveness as newly manufactured products.

It was believed that this requirement would impose tremendous financial burdens upon the medical device industry, and, if implemented, would require that products returned for repair, independent of age, much be made to attain all of the characteristics of current production.

The Commissioner agrees with the comments and has deleted this requirement from the proposed regulations.

The Commissioner has carefully considered the environmental effects of the proposed regulation and, because the proposed action will not significantly affect the quality of the human environment, has concluded that an environmental impact statement is not required.

The inflationary impact of the proposed good manufacturing practice regulations for medical devices was carefully considered in accordance with Executive Order No. 11821, OMB Circular A–107, and the guidelines issued by the Department of Health, Education, and Welfare. The Commissioner had determined that the agency lacks the data that are needed to perform a valid assessment at this time and consequently he is deferring judgment on whether or not these regulations are likely to cause a major inflationary impact.

The Commissioner asks that interested and informed parties submit data in a form which is adaptable to the analytic framework documented in the "Preliminary Inflation Impact Review of the Pro-

posed Good Manufacturing Practices Regulations for Medical Devices," on file with the Hearing Clerk, Food and Drug Administration.

Economic data should address one or more of the following areas:

a. Medical device industry characteristics, such as annual revenues, employment, firm size distribution, etc.

b. Present levels of quality control costs (pre-manufacturing and production phases) and future levels anticipated as a result of these proposed regulations, as a percentage of annual sales.

c. Present levels of failure costs, for correcting defects before and after shipment and for fulfillment of guarantees, and future levels anticipated as a result of these proposed regulations.

d. Types of products manufactured and whether they are critical or noncritical devices.

e. Annual sales.

f. Numbers of employees (if any) that would be hired or released as a result of these proposed regulations.

g. Competitive advantage or disadvantage attributed to the proposal.

To the extent possible, respondents should cite the specific sections of the proposal, such as: Cleaning and sanitation, distribution records, device labeling, etc., and the special circumstances, if any, that account for any estimated economic impact. The Commissioner is particularly interested in learning whether the disparity between present and expected future costs is attributable to a company's belief that an existing quality control program is not in compliance with the proposed regulations or would be unlikely to be granted an exemption or variance.

The agency's subsequent analysis of the inflationary impact of the regulations will be based on data received and its availability for public examination and further comment will be announced in the FEDERAL REGISTER before any final regulations are promulgated.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 501, 502, 518, 519, 520(f), and 701(a) as amended, 52 Stat. 1049–1051 as amended, 1055, 90 Stat. 562–565, 567–569 (21 U.S.C. 351, 352, 360(h), 360(l), 360j(f) 371(a)) and under authority delegated to the Commissioner (21 CFR 5.1) (recodification published in the FEDERAL REGISTER of June 15, 1976 (41 FR 24262)), it is proposed that Chapter I of Title 21 of the code of Federal Regulations be amended by adding new Part 820 to read as follows:

PART 820—GOOD MANUFACTURING PRACTICE FOR MEDICAL DEVICES; GENERAL

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820.191 Critical devices, quality control manual.
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820.198 Complaint files.

AUTHORITY: Sec. 501, 502, 518, 519, 520(f), 701(a), 52 Stat. 1049–1051 as amended, 1055, 90 Stat. 562–565, 567–569 (21 U.S.C. 351, 352, 360h, 3601, 360j(f), 371(a)).

Subpart A—General Provisions

§ 820.1 Scope.

The regulations set forth in this part describe current good manufacturing practice for methods used in, and the facilities and controls used for, the manufacture, packing, storage, and installation of all devices for human use to assure that the device will be safe and effective and otherwise in compliance with the Federal Food, Drug, and Cosmetic Act. This Part 820 establishes basic requirements applicable to all devices for human use and additional requirements for critical devices. Every device manufacturer shall comply with the applicable provisions of this part and prepare and implement procedures complementing this regulation that are appropriate to the specific device manufactured.

(a) *Authority.* This Part 820 is established and promulgated under authority of sections 501, 502, 518, 519, 520(f), and 701(a) of the act (21 U.S.C. 351, 352, 360h. 3601, 360j(f), and 371(a)). The failure to comply with any regulation in this part in the manufacture, packaging, storage, or installation of a device renders the device adulterated under section 501(h) of the act. Such a device, as well as the person responsible for the failure to comply, is subject to regulatory action.

(b) *Limitations.* The current good manufacturing practice regulations in this part supplement regulations in other parts of this chapter except where explicitly stated otherwise. In the event it is impossible to comply with applicable regulations both in this part and in other parts of this chapter, the regulations specifically applicable to the device in question shall supersede any other regulation.

(c) *Applicability.* The provisions of this Part 820 shall be applicable to any device, as defined in the act, that is manufactured, imported or offered for import in any State or Territory of the United States, the District of Columbia, and the Commonwealth of Puerto Rico.

§ 820.3 Definitions.

(a) "Act" means the Federal Food, Drug, and Cosmetic Act, as amended (secs. 201–902, 1040 et seq. as amended (21 U.S.C. 321–392)).

(b) "Automated quality control" means any system used in the quality control decisionmaking functions that uses a computer or other apparatus for performing quality control functions independent of, or semi-independent of, manual control.

(c) "Component" means any material, substance, piece, part, or assembly intended for use during the manufacturing of a device which will appear in the finished product.

(d) "Control number" means any combination of letters and numbers from which the complete history of components, manufacture, control, packaging, sterilization, and distribution of the device can be determined; the control number may be in the form of designations such as "production run," "lot," "batch," "data code," or "serial number."

(e) "Critical component" means an individually identifiable component, assembly, or subassembly of a critical device that has a potential to cause a device failure or affect the safety, performance, or effectiveness of a critical device.

(f) "Critical device" means a device intended to support or sustain life or intended for surgical implant into the body, whose failure could result in permanent injury to the user, or which has been declared a critical device by the Commissioner after consultation with the Device Good Manufacturing Practice Advisory Committee authorized under section 520(f) of the act.

(g) "Critical operation" means any operation in the manufacture of a critical device that has a potential to cause a device failure or adversely affect the safety, performance, or effectiveness of a critical device.

(h) "Finished device" means a device, or any accessory to a device, that is ready to be used for its intended purpose whether or not packaged or labeled for commercial distribution: for example, a hemodialysis unit, disposable hemodialysis tubing, blood filters, syringes, needles, or diagnostic reagents.

(i) "Manufacturer" means any person(s), including repackers and relabelers, who manufactures, fabricates, assembles, or processes a device in whole or in part. It does not include those to whom the device is subsequently delivered or sold solely for distribution of the device in commerce.

(j) "Manufacturing material" means any material intended for use during the manufacture of a device but which is not intended to appear in the finished product, e.g., cleaning, mold-release, and lubricating agents.

(k) "Noncritical device" means all devices other than those designated as critical devices.

(l) "Quality control unit" means any organizational element of the manufacturer having authority and responsibility in accordance with § 820.20.

Subpart B—Organization and Personnel

§ 820.20 Organization.

The organization of each device manufacturer shall include a quality control unit which shall consist of one or more persons with the responsibility and the authority to perform formally established and documented quality assurance programs. Such a unit shall have the freedom to identify, initiate, recommend, or provide solutions to quality assurance problems and to verify the implementation of such solutions. Any unit that checks, audits, or otherwise verifies correct performance of operations shall be independent of the unit performing that operation.

(a) *Responsibilities of the quality control unit.* The quality control unit shall have the responsibility and authority to approve or reject all components, manufacturing materials, in-process materials, packaging materials, labeling, and finished devices and to review production records. It shall also be responsible for performing inspection checks during the manufacture of a device as set forth in the quality control manual, and also be responsible for approving or rejecting devices manufactured, processed, packed, or held under contract by another company.

(b) *Audit.* Planned and periodic audits of the quality assurance system shall be implemented to verify compliance with the effectiveness of the quality assurance program. The audits shall be performed in accordance with written procedures by appropriately trained individuals not having direct responsibilities in the areas being audited. Audit results shall be documented and reviewed by management having responsibility in the area audited. Followup action, including reaudit of deficient areas, shall be taken when indicated.

§ 820.25 Personnel.

There shall be sufficient personnel having the educational background, training, and experience necessary to ensure that their functions are adequately performed.

(a) *Personnel training.* All personnel shall have a thorough understanding of the functions they perform, necessary training and experience, and adequate information concerning applicability of their functions to pertinent provisions of this part. Quality control personnel shall be made aware of defects and errors likely to be encountered in their individual control function through a documented training program.

(b) *Personnel health and cleanliness.* Personnel in contact with the device or its environment shall be clean, healthy, and suitably attired to the extent that these factors may affect the finished device. Any personnel who by medical examination or supervisory observation appears to have a condition which could adversely affect the device shall be excluded from affected operations until the condition is corrected. Personnel with such conditions shall be instructed to report them to supervisory personnel.

Subpart C—Buildings

§ 820.40 Buildings.

Buildings in which manufacturing, assembling, packaging, packing, holding, testing, and labeling operations are conducted shall be of suitable design and contain sufficient space to facilitate adequate cleaning, maintenance, and other necessary operations. The facilities shall provide adequate space to prevent mixups and to assure orderly handling of the following: Incoming components; rejected or obsolete components; in-process components; finished devices; labeling; reprocessed, reworked and repaired devices; equipment; molds, patterns, tools, records, drawings, blueprints; testing and laboratory operations; and quarantined products.

§ 820.46 Environmental control.

Environmental conditions shall be controlled when necessary to prevent contamination and to provide proper conditions for each of the operations performed in each building pursuant to § 820.40. Conditions to be considered for control are lighting, ventilation, temperature, humidity, air pressure, airborne and other contamination, screening, and filtration. Periodic verification of environmental controls shall be performed and documented.

§ 820.56 Cleaning and sanitation.

There shall be adequate cleaning and sanitation to meet process requirements, including the following:

(a) *Personnel sanitation.* Washing and toilet facilities shall be clean and adequate. Clean dressing rooms shall be provided when necessary.

(b) *Vermin, pest, and insect control.* Procedures to control vermin, pests, and insects and safeguards to prevent contamination of equipment, components, in-process components, or finished devices by rodenticides, insecticides, fungicides, fumigants, hazardous substances, and other cleaning and sanitizing substances shall be documented.

(c) *Personnel practices.* Eating, drinking, and smoking by personnel shall be limited to designated areas, where necessary.

(d) *Sewage and refuse disposal.* Sewage, trash, by-products, chemical effluents, and other refuse shall be disposed of in a safe and sanitary manner.

(e) *Written cleaning procedures and schedules.* Written cleaning procedures and schedules shall be made available to appropriate personnel. Any special area requirements or warnings shall be posted.

Subpart D—Equipment

§ 820.60 Equipment.

Equipment used in the manufacturing process shall be appropriately designed, constructed, placed, and installed to facilitate maintenance, adjustment, and cleaning. All manufacturing materials or other substances used with such equipment or which may come in contact with the device shall not adversely affect the device.

(a) *Maintenance schedule.* There shall be, if applicable, a schedule for maintaining, adjusting, and cleaning the equipment. Such schedules shall be visibly posted on or near each piece of equipment, or be readily available to personnel performing these functions. A written record of these activities shall be maintained.

(b) *Inspection.* Periodic documented inspections shall be made of all equipment to ensure adherence to such schedules and to make certain the equipment is in the proper state of cleanliness and operating tolerances.

(c) *Adjustment.* Any inherent limitations or allowable tolerances shall be visibly posted on or near equipment requiring periodic adjustment.

(d) *Manufacturing materials.* Manufacturing materials including cleaning agents, mold-release agents, lubricating, or other substances used on or in the manufacturing equipment or the device shall be subsequently removed from the device or limited to specified amount that does not adversely affect the safety or effectiveness of the device. The use and removal of such manufacturing materials shall be documented.

§ 820.61 Measurement equipment.

All measurement equipment used for production and quality control shall have the capability of measuring to a degree of accuracy suitable for the intended purpose and have the capability of providing valid results. Documented periodic inspections shall be made of such measurement equipment to assure that it is maintained to the necessary degree of accuracy.

(a) *Production measurement equipment.* Production jigs, fixtures, tooling masters, templates, patterns, and other such inspectional standards shall be standardized prior to initial use and at periodic intervals. Such standardization shall be documented.

(b) *Automated quality control.* The following factors are pertinent in the documentation of design validity for automated quality control equipment:

(1) *Design of function.* The manufacturer shall determine the validity of the automated test and whether the method

will produce results directly applicable to the device being tested.

(2) *System compatibility.* All components of an instrument or equipment system used for quality control testing of a device shall be compatible with each other.

(3) *Programming.* When computers are used as part of an automated quality control system, the programs shall be verified by adequate and documented testing. Only designated personnel shall make program changes through a formal approval procedure.

§ 820.62 Critical devices, measurement equipment.

In addition to the requirements of § 820.61, the calibration of all measurement equipment used in the quality control program related to critical devices shall be traceable to the prime standards at the National Bureau of Standards, Department of Commerce. If prime standards do not exist for the parameter being measured, an independent reproducible standard shall be used. If none of the above exist, an in-house primary standard shall be developed and used.

§ 820.68 Equipment calibration.

Automatic, mechanical, or electronic measurement equipment used in the manufacturing of a device shall be routinely calibrated, inspected, or checked according to written procedures containing specific directions, schedules, limits for accuracy and precision, and provisions for remedial actions in the event accuracy and/or precision limits are not met. Written records of those calibration checks and inspections shall be maintained.

(a) *Calibrator.* Calibration shall be done only by persons having sufficient training, knowledge, and experience.

(b) *Calibration record.* The date of calibration, the individual performing it, and the calibration due date shall be indicated on each piece of equipment. A designated individual shall maintain a separate record showing calibration dates, methods, data, and by whom calibrated.

Subpart E—Control of Components, Containers, and In-Process Materials

§ 820.80 Components.

Components used in manufacturing a device shall be received, stored, and handled in a manner designed to prevent damage, mixup, contamination, or other adverse effect. Components shall be quarantined prior to acceptance or clearly identified as not yet accepted.

(a) *Acceptance of components.* There shall be a written procedure for acceptance of components. A designated individual shall maintain records of component acceptance and rejection. Upon receipt, each shipping container of components shall be visually examined for damage. When appropriate, components shall be inspected, sampled, and tested for conformance with specifications.

(b) *Storage and handling of components.* Components shall be stored in a manner designed to facilitate appropriate stock rotation procedures. Component control numbers or other identifications shall be easily viewable. All obsolete and rejected components shall be segregated from acceptable components and clearly identified. Records shall be maintained of all obsolete and rejected components.

§ 820.81 Critical devices, components.

In addition to the requirements of § 820.80, the following are required:

(a) *Acceptance of critical components.* All critical components shall be representatively sampled for testing and examination. The number of containers sampled and the amount to be taken from each container shall be based upon appropriate statistical criteria, the past quality history of the supplier, and the quantity needed for analysis and reserve. All critical components shall be identified with control numbers upon receipt. The rejection percentages for all critical device components shall be maintained by a designated individual and identified by supplier name.

(b) *Component supplier agreement.* There shall be a written agreement between the critical component supplier and the device manufacturer whereby the supplier agrees to notify the manufacturer of any subsequent change in a component, component test, inspection or procedure. Where such an agreement exists, the manufacturer shall not accept such a change until he determines the impact of the change on the finished device.

Subpart F—Production and Process Controls

§ 820.100 Manufacturing specifications and processes.

Written manufacturing specifications and processing procedures shall be designed, implemented, and supervised to assure that the device manufactured is consistent with specified procedures and the requirements of this part.

(a) *Specification controls.* (1) Specification control measures shall be established to assure that the design basis for devices, components, and packaging is correctly translated into approved specifications.

(2) Specification changes, including changes made concerning devices already distributed shall be subject to control measures as great as or greater than those applied to the original design before the changes and shall be approved by designated individuals. All such approvals of specification changes shall be documented and shall state the date of approval and the date the change becomes effective.

(3) To assure conformance with specifications, written testing and sampling procedures shall described in-process controls to be used when appropriate. The procedure shall be contained in the quality control manual under § 820.190.

(b) *Processing controls.* (1) All operations in the processing of a device shall be controlled in a manner designed to assure that the device conforms to applicable specifications.

(2) There shall be a formal approval procedure for any change in the manufacturing process of a device. Such changes shall be made available to appropriate personnel.

(c) *Trend analysis.* When appropriate, there shall be an ongoing trend analysis of components and finished devices to indicate statistical control of a process.

§ 820.101 Critical devices, manufacturing specifications and processes.

In addition to the requirements of § 820.100, the following critical operation controls shall apply:

(a) *Critical operation performance.* Critical operations shall be performed by designated individuals or equipment and shall be suitably verified.

(b) *Record of critical operation.* The individual performing a critical operation shall record that operation in the device history record as required in § 820.185. Such record shall identify the date performed, operator identification, and when appropriate, the major equipment used. Any individual checking a critical operation shall indicate the date checked, name of the checker, and when appropriate, identification of checking equipment used. The information shall be recorded immediately upon the completion of the operation or the check or at suitable intervals compatible with the operational process.

(c) *Critical components.* There shall be a device history record which shall identify each critical component of the device and shall include the information required in § 820.185.

§ 820.115 Reprocessing of devices or components.

(a) All finished device units rejected during finished device inspection and later reprocessed are subject to another complete final inspection.

(b) Reprocessing procedures shall be so devised, implemented, and supervised to assure that subsequent finished devices meet the original, or subsequently modified and approved, specifications.

§ 820.116 Critical devices, reprocessing of devices or components.

In addition to the requirements of § 820.115, the following reprocessing controls shall apply:

(a) *Reprocessing procedures.* There shall be written procedures for any reprocessing associated with the production of a critical device or component. These procedures shall indicate the design, equipment, and special reprocessing factors, such as change in material due to constant reprocessing, to assure that the reprocessed device or component meets approved specifications. The procedures shall include any special quality control methods or tests. The reprocessing procedures shall be designed so that the reprocessed device or component meets the same or equal specifications as the original device or component. Adulteration because of material, structural and molecular change due to reprocessing, and other like considerations must be addressed in the procedures. Special

care shall be taken to assure that the device or component to be reprocessed is clearly identified and separated from like devices or components not to be reprocessed. When there is a continual reprocessing of a component, such as waste from forms, dyes, etc., a determination of the effect of the reprocessing upon the component shall be made and documented. There shall be a formal approval procedure for instituting a new, or altering an approved, reprocessing procedure.

(b) *Reprocessing control.* Any reprocessed critical device or component shall conform to specifications of the original device or component. Written testing and sampling procedures to assure such conformity shall be contained in the quality control manual as required in § 820.191. Any prior quality control check shall be repeated on the reprocessed device or components if reprocessing could affect the specifications previously inspected. When it is necessary to reprocess a device or component rejected for other than a physically visible defect, appropriately quality control inspection shall be performed for all specifications.

(c) *Failure investigation.* The failure of a critical device or any of its components to meet specifications shall be thoroughly investigated. The investigation shall be conducted for distributed and undistributed devices and shall extend to other devices that may have been associated with the specific failure or discrepancy. A written record of the investigation shall be made including conclusions and followup.

Subpart G—Packaging and Labeling Control

§ 820.120 Device labeling.

There shall be adequate controls to maintain labeling integrity and to prevent labeling mixups.

(a) *Label integrity.* Labels shall be designed, printed, and applied so as to remain legible and attached to the device during the customary conditions of storage, distribution, and use.

(b) *Separation of operations.* Each labeling and packaging operation shall be separated physically or spatially in a manner designed to prevent mixups.

(c) *Area inspection.* Prior to the implementation of any labeling and packaging operation, there shall be an inspection of the area by a designated individual, other than the operator, to assure that devices and labeling materials from prior operations do not remain in the labeling or packaging area. Any such items found shall be destroyed, disposed of, or returned to storage prior to onset of a new or different labeling of packaging operation. A record of such inspection, including the date and person performing the inspection, shall be recorded in the device history record.

§ 820.121 Critical devices, device labeling.

In addition to the requirements of § 820.120, labeling materials issued for critical devices shall be examined for identity, including the presence of the correct expiration date, control number, storage instructions, handling instructions, and additional processing instructions, where applicable. The following are controls for critical device labels and labeling:

(a) *Labeling receipt.* Labels and other labeling shall not be released to inventory until a designated individual proofreads for accuracy a statistically selected sample against an approved final copy. The date and signature of the individual proofreading the labeling shall be recorded.

(b) *Storage.* Labels and labeling shall be stored and maintained in a manner which provides proper identification and prevents mixups.

(c) *Access restriction.* Access to labels and labeling shall be restricted to authorized personnel.

(d) *Excess printed labels.* All excess printed labels bearing control numbers shall be destroyed or appropriately altered at the conclusion of the packaging and labeling operation.

§ 820.130 Device packaging.

Package design, construction, and material shall be adequate to protect the device during customary conditions of processing, storage, handling, and shipment.

§ 820.131 Critical devices device packaging.

In addition to the requirements in § 820.130, for critical devices the following are required:

(a) *Device package design.* The device package shall be designed and constructed to protect the device from alteration or damage by expected external factors. When a form of external energy such as electromagnetic energy, heat, cold, or pressure could alter, damage, or otherwise adversely affect the device, the package shall be so designed and constructed to withstand the influx of such levels of energy as may be reasonably anticipated.

(b) *Storage and handling protection.* The device containers and packages shall be designed to withstand any reasonably anticipated factors to be encountered under normal and common storage and handling conditions of the device until ready for its intended use.

Subpart H—Holding and Distribution

§ 820.150 Distribution.

There shall be written procedures for finished device warehouse control and distribution to assure that only those devices authorized for release are distributed. Where appropriate, there shall be a system whereby the oldest approved devices are distributed first.

§ 820.151 Critical devices, distribution records.

In addition to the requirements of § 820.150, for critical devices adequate distribution records shall be maintained and made readily available. Such records shall include the name and address of the consignee, the name and quantity of devices, date shipped, and the control number used. These records shall be retained as required by § 820.180(b).

Subpart I—Product Evaluation

§ 820.160 Finished device inspection.

There shall be written procedures for finished device inspection to assure that specifications applicable to the finished device have been met. Prior to release for distribution, each production unit, lot, run, or control number shall be checked, including testing where necessary, for conformance with device specifications. A device shall be tested under those conditions in which it is expected to operate, e.g., temperature, humidity, pressure. Sampling plans used for testing and release of a device shall be statistically validated. Where appropriate, finished devices shall be held in quarantine until released.

§ 820.161 Critical devices, finished device inspection.

In addition to the requirements of § 820.160, a finished critical device shall not leave the control of the manufacturer for distribution until all acceptance records and test results are checked by a designated individual. Such individual shall assure that all records and documentation required for the device history record are present, complete, and correct, and shall authorize, by signature, the release of the finished device for distribution.

Subpart J—Records and Reports

§ 820.180 General requirements.

Except as specifically provided elsewhere, the following general provisions shall apply to all records required by this part. Required records include those listed in this subpart as well as records referred to in other subparts of Parts 820 through 829.

(a) *Confidentiality.* Those records deemed confidential by the manufacturer may be marked to aid the Food and Drug Administration in determining whether data and information may be disclosed under the public information regulation in Part 4 of this chapter.

(b) *Record retention period.* All required records pertaining to a device shall be retained for a period of time consistent with the design and expected life of the device, or other reasonably valid time period established by the manufacturer, but in no case less than 2 years from the date of release for commercial distribution by the manufacturer.

§ 820.181 Master device record.

The master device record, a compilation of records pertaining to the design and specifications of a device, shall be prepared, dated, and signed by a designated individual. The master device record shall include all specifications and procedures or appropriate references for each separate device entity. Any changes in the master device record shall be recorded with an authorizing signature. Any formal approval forms shall be a part of the master device record.

§ 820.182 Critical devices, master device record.

In addition to the requirements of § 820.181, for critical devices the master device record shall include the following specific material or references to the location of such materials:

(a) *Device specification.* The complete device specification documentation, including drawings, composition, formulation, and component specifications.

(b) *Production process specifications.* The complete production process specifications, including equipment specifications, production methods, production procedures, and production environment specifications.

(c) *Quality control specifications.* The complete quality control specifications, including the quality control checks utilized and the quality control apparatus used.

(d) *Critical components and critical component suppliers.* Full information concerning critical components and critical component suppliers, including the complete specifications of all critical components, the sources from whom they may be obtained, and written copies of any agreements made with suppliers.

(e) *Control number.* The manufacturer shall designate a production unit, which is identifiable under a unique control number, for purposes of traceability. The production unit may be production run, lot, batch, date code, serial number, or other designation.

(f) *Label and labeling.* Complete labeling procedures for the individual device and copies of all labels, labeling, and any promotional material.

(g) *Packaging specifications.* The complete packaging specifications, including methods and processes.

§ 820.184 Device history record.

Sufficient records shall be maintained to demonstrate that the device conforms to specifications.

§ 820.185 Critical devices, device history record.

In addition to the requirements of § 820.184, for critical devices there shall be a device history record for each control number which shall include complete information relating to the production and control of each production unit. This record shall identify the specific label, labeling, and control number used on each production unit and shall be readily accessible and maintained by a designated individual. The device history record shall include or reference:

(a) *Operation documentation.* The documentation of each critical operation performed in the manufacturing of a device, including the date performed, major equipment used, and signatures of performing and checking individuals.

(b) *Component documentation.* Documentation of each critical component used in the manufacturing of a device. This shall include:

(1) *Control number.* The control number of the critical components used in the manufacturing of a device.

(2) *Acceptance record.* The acceptance record of the component with signature of accepting individual.

(3) *Movement to/from storage.* The date each component was accepted into the storage area, the date moved into the production area, and the signature of the accepting individual.

(c) *Inspection checks.* The inspection checks performed, the methods and equipment used, results, and the date and signature of the inspecting individual.

§ 820.190 Quality control manual.

There shall be a manual containing written procedures or references for quality control inspection, specification checks, tooling, and standards covering each device.

§ 820.191 Critical devices, quality control manual.

In addition to the requirements of § 820.190 and other provisions of this part, for critical devices the quality control manual shall record or reference:

(a) *Device and component specifications.* All device and component specifications to be checked by the quality control unit.

(b) *Inspection checks.* The validated methods and equipment to be used for inspection checks.

(c) *Formal change approval.* A formal approval procedure for any change in the quality control of a device.

(d) *Sampling plan.* A description of each sampling plan utilized.

§ 820.195 Critical devices, automated data processing.

When automatic data processing is utilized, adequate checks shall be designed to prevent inaccurate data output, input, and programming errors. A duplicate copy of computerized information relating to the requirements of this part shall be made and stored in a separate geographical location. Hard copy reports shall be provided if requested by Food and Drug Administration representatives.

§ 820.198 Complaint files.

(a) Written and oral complaints representing any dissatisfaction relative to the identity, quality, durability, reliability, effectiveness, or performance of a device shall be reviewed by the quality control unit. This unit shall determine whether or not an investigation is necessary. Any complaint involving the possible failure of a device to meet any of its specifications shall be investigated in accordance with § 820.116(c).

(b) A written record of each complaint and investigation shall be maintained in a file designated for device complaints. The written records shall include the name of the device, control number, name of complainant, nature of complaint and reply to complainant. All complaints pertaining to injury, death, or any hazard to safety shall be maintained in a separate portion of the complaint file and shall be immediately reviewed and evaluated by a designated individual.

(c) When an investigation is made, the record shall include the findings of the proceedings and followup. When no investigation is made, the record shall include the reason and the name of the person responsible for such determination.

Interested persons may on or before June 29, 1977, submit to the Hearing Clerk, Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20857, written comments (preferably in quintuplicate and identified with the Hearing Clerk docket number found in brackets in the heading of this document) regarding this proposal. Received comments may be seen in the above office between the hours of 9 a.m. and 4 p.m., Monday through Friday. Ordinarily, 60 days is provided for comment on a proposal, but the Commissioner may reduce or extend this time period for good cause. Because of the nature and extent of the regulations being proposed, the Commissioner has concluded that 120 days should be allowed for public comments. In the absence of extraordinary circumstances, no extension of time for comment will be granted.

The inflationary impact of the proposed good manufacturing practice regulations for medical devices was carefully considered in accordance with Executive Order No. 11821, OMB Circular A–107, and the guidelines issued by the Department of Health, Education, and Welfare. The Commissioner had determined that the agency lacks the data that are needed to perform a valid assessment at this time and consequently he is deferring judgment on whether or not these regulations are likely to cause a major inflationary impact.

Dated: February 23, 1977.

SHERWIN GARDNER,
Acting Commissioner of Food and Drugs.

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